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Variant: NM_001110792.2(MECP2):c.1376C>T (p.Ala459Val)

Version: 1.0

CA270277

143466 (ClinVar)

Gene: MECP2 (HGNC:4204)
Condition: Rett syndrome (MONDO:0010726)
Inheritance Mode: X-linked inheritance
UUID: cb5510b0-4ce3-421c-9eda-b36752839e3a
Approved on: 2026/4/23
Published on: 2026/6/26

HGVS expressions

NM_001110792.2(MECP2):c.1376C>T (p.Ala459Val)
NM_001110792.2:c.1376C>T
NC_000023.11:g.154030488G>A
CM000685.2:g.154030488G>A
NC_000023.10:g.153295939G>A
CM000685.1:g.153295939G>A
NC_000023.9:g.152949133G>A
NG_007107.2:g.111640C>T
NG_007107.3:g.111616C>T
ENST00000303391.11:c.1340C>T
ENST00000453960.7:c.1376C>T
ENST00000303391.10:c.1340C>T
ENST00000453960.6:c.1376C>T
ENST00000619732.4:c.1340C>T
ENST00000628176.2:c.*712C>T
NM_001110792.1:c.1376C>T
NM_001316337.1:c.1061C>T
NM_004992.3:c.1340C>T
NM_001316337.2:c.1061C>T
NM_001369391.2:c.1061C>T
NM_001369392.2:c.1061C>T
NM_001369393.2:c.1061C>T
NM_001369394.1:c.1061C>T
NM_001369394.2:c.1061C>T
NM_001386137.1:c.671C>T
NM_001386138.1:c.671C>T
NM_001386139.1:c.671C>T
NM_004992.4:c.1340C>T

Benign

Met criteria codes 2

BS2 BS1

Evidence Links 0

Expert Panel

Rett and Angelman-like Disorders VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Rett and Angelman-like Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for CDKL5 Version 5.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The highest population minor allele frequency of the p.Ala447Val variant in MECP2 (NM_004992.4) in gnomAD v4.1 is 0.000030 in Non-Finnish European population, which is higher than the ClinGen Rett and Angelman-like Disorders VCEP threshold (≥0.0000083) for BS1, and therefore meets this criterion (BS1). The p.Ala447Val variant is observed in at least 2 unaffected individuals (internal database - GeneDx) (BS2). In summary, the p.Ala447Val variant in MECP2 is classified as benign based on the ACMG/AMP criteria (BS1, BS2). (MECP2 Specifications v5.0; curation approved on 4/23/2026)

Met criteria codes

BS2	✔	The p.Ala447Val variant in MECP2 (NM_004992.4) is observed in at least 2 unaffected individuals (internal database - GeneDx) (BS2).
BS1	✔	The highest population minor allele frequency of the p.Ala447Val variant in MECP2 (NM_004992.4) in gnomAD v4.1 is 0.000030 in Non-Finnish European population, which is higher than the ClinGen Rett and Angelman-like Disorders VCEP threshold (≥0.0000083) for BS1, and therefore meets this criterion (BS1).

Curation History

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